

## REMARKS

Claims 4-10, 14, 15 and 18 are pending the application; Claims 4-10, 14, 15 and 18 stand rejected. By this Amendment, Claims 5 and 18 have been cancelled and Claims 4, 6-10 and 15 have been amended. These amendments add no new matter to the application.

The Examiner has objected to, and required correction of, all claims drawn to any sulfated macromolecule other than heparan sulfate; Claim 18 has been cancelled without prejudice at this time, and Claim 10 has been amended to refer only to heparan sulfate.

Various claims stand objected to as allegedly indefinite, and all such claims are now amended to address these concerns. For instance, Claim 4 now recites co-incubation, as suggested; Claims 6-7 and 8-9 recite a molar ratio, and a weight ratio, respectively, as suggested.

The Examiner has also objected to Applicant's standard usage of the term "about"; Applicant respectfully traverses this objection, and points out that artisans have been writing technical claims with this term, with the approval of the courts of appeal, for many years. In brief, the courts say that when artisans know what they mean amongst themselves in using this term, and this approximation is supported in the specification, then the term is not vague or indefinite. Artisans would understand at the least that, as the Examiner also seems to understand, the term 'about' in this case, means 'approximately'. In this case, the term is well supported in the specification, and persons skilled in this art can readily deduce what would fit within the range of the term 'about' and what would not. Applicant therefore requests reconsideration of this objection and allowance of the objected to claims.

Claims 4-10, 14-15 and 18 stand rejected under 35 USC 112 as allegedly indefinite; Applicant respectfully traverses this rejection. Nonetheless, Claim 18 has been cancelled without prejudice at this time, and Claim 10 has been limited at this time to heparan sulfate, with no

exclusion. The rejections therefore appear to be moot at this time. Reconsideration and allowance are requested.

Claims 4-10, 14-15 and 18 stand rejected under 35 USC 102 as allegedly anticipated by the Snow reference or the Castillo reference, respectively; Applicant respectfully traverses these rejections. First of all, both of the cited reference authors are the inventors of record in the present case, and it is therefore believed to be improper to cite references authored by them in the same field. Withdrawal of these rejections is therefore requested.

Alternatively, and not exclusively, the Snow reference actually teaches away from the claimed method. The Snow reference only teaches formation of amyloid star plaques with A $\beta$  and perlecan, not the presently claimed A $\beta$  and heparan sulfate; in fact, heparan sulfate GAGs were then thought actually to inhibit formation of star plaques (see page 229). In 1994, it was thought that only intact core perlecan could form star plaques. The figures referred to by the Examiner are only electron micrographs (in which the signature 'star' plaque configuration does not show in any case). The Examiner is referred instead to specification figures 6a, 6b and 7a for true star, or Maltese cross, configuration illustrations created with the claimed heparan sulfate.

The Castillo reference is believed to have been published less than one year before the 3/13/98 earliest priority date of this application, and is therefore not applicable to this case. Alternatively, the Examiner is asked to consider that Castillo was reporting on binding studies only, not on plaque formations, and he says at page 2461, second paragraph, that EHS perlecan (which was used then in the study) could not be made to form plaques at all! It must be distinguished, as to the Castillo reference, that not everything that binds forms plaques, and not every plaque is the preferred Maltese cross plaque, with "Maltese-cross pattern when stained with Congo red and viewed under polarized light, and an amyloid star appearance when viewed by transmission electron microscopy" which is the limitation as claimed. In addition it should be

noted that Castillo at page 2460, in his figure 8, further teaches that many substances, when combined with A $\beta$ , fail to create and demonstrate the claimed maltese cross plaques; for instance, alpha1-antichymotrypsin, C3 and P component (see description in Castillo for further identification of these substances) were actually significant inhibitors of the maltese cross formation.

Since neither the Snow nor the Castillo reference teaches or suggests all of the limitations as claimed, neither one, nor both of the references can fairly be said to anticipate the claims, and Applicant requests reconsideration and allowance of these claims.

Applicant believes that it has responded fully to all of the concerns expressed by the Examiner in the Office Action, and respectfully requests reexamination of all rejected claims and early favorable action on them as well. If the Examiner has any further concerns, Applicant requests a call to Patrick Dwyer at (206) 343-7074.

Respectfully submitted,



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P08-OA3.RSP